SAFETY DATA SHEET

Product Name: Irinotecan Hydrochloride Injection

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Name And Address	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA	Hospira Australia Pty Ltd 1 Lexia Place Mulgrave VIC 3170 AUSTRALIA
Emergency Telephone #'s	CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia - 61-290372994; UK - 44-870-8200418	
Hospira, Inc., Non-Emergency	224 212-2000	
Product Name	Irinotecan Hydrochloride Injection	
Synonyms	***(S)***-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo1*H*pyrano[3',4':6,7]-indolizino[1,2-b]quinolin-9-yl-[1,4'bipiperidine]-1'-carboxylate, monohydrochloride, trihydrate; (+)-7-Ethyl-10-hydroxycamptothecine 10-[1,4'-bipiperidine]-1'-carboxylate hydrochloride trihydrate.	

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Irinotecan Hydrochloride Injection is a solution containing irinotecan hydrochloride. Clinically, it is used to treat certain types of cancers. It is a cytotoxic agent, and in the workplace, should be considered a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, cardiovascular system, lungs, and liver.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Not Classified	Not Classified

Health Hazards	**Hazard Class**	**Hazard Category**
	Toxic to Reproduction	2
	Germ Cell Mutagenicity	2
	STOT – RE	2

Label Element(s)

Pictogram

Signal Word

Warning

Hazard Statement(s)

Suspected of damaging fertility or the unborn child
Suspected of causing genetic defects
May cause damage to organs through prolonged or repeated exposure

2. HAZARD(S) IDENTIFICATION: continued

Precautionary Statement(s)

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Irinotecan Hydrochloride
Chemical Formula $C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Irinotecan Hydrochloride Trihydrate	2	136572-09-3	NA

Non-hazardous ingredients include Water for Injection and 4.5% sorbitol. Hazardous ingredients present at less than 1% include lactic acid; sodium hydroxide and/or hydrochloric acid, which are added to adjust the pH.

4. FIRST AID MEASURES

Eye Contact

Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/ supportive care as necessary.

Skin Contact

Remove from source of exposure. Flush with copious amounts of water. If irritation occurs or signs of toxicity occur, seek medical attention. Provide symptomatic/ supportive care as necessary.

Inhalation

Remove from source of exposure

Ingestion

Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Prophylactic or therapeutic administration of 0.25 to 1 mg of intravenous or subcutaneous atropine may be considered (unless clinically contraindicated) in employees experiencing rhinitis, increased salivation, miosis, lacrimation, diaphoresis, flushing, abdominal cramping, or diarrhea (occurring during or shortly after exposure to irinotecan. These symptoms are expected to occur more frequently with higher irinotecan exposures.

5. FIRE FIGHTING MEASURES

Flammability

None anticipated for this aqueous product.

Fire & Explosion Hazard

None anticipated for this aqueous product.

Extinguishing Media

As with any fire, use extinguishing media appropriate for primary cause of fire such as carbon dioxide, dry chemical extinguishing powder or foam.

Special Fire Fighting Procedures

No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal

Isolate the area around the spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb liquid with suitable material and clean the affected area with soap and water. Application of household bleach for 10 minutes can be used to further clean the affected spill areas. Dispose of all spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Irinotecan hydrochloride, the active ingredient in the formulation, is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastics agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. When handling the powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this material.

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert. Upon dilution, photodegradation of irinotecan hydrochloride is accelerated in neutral and alkaline solutions compared with acidic solutions. At pH 10, photodegradation is very rapid while at pH 3, photodegradation is much slower. At pH 7, a 0.34 mg/mL aqueous solution of irinotecan degraded 32% in six hours when exposed to a daylight lamp, and 19% when exposed to a white fluorescent light.

Special Precautions

No special precautions required for hazard control. Persons with known hypersensitivities to irinotecan hydrochloride, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling open containers of this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Irinotecan Hydrochloride	8-hr TWA: Not established	8-hr TWA: Not established	8-hr TWA: Not Established	8-hr TWA: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8-hour Time Weighted Average.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION: continued

Respiratory Protection	Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.
Skin Protection	When handling this material, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.
Eye Protection	As a minimum, the use of chemical safety goggles is recommended when handling this material.
Engineering Controls	When handling this material, local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A pale yellow, clear, aqueous solution
Odor	NA
Odor Threshold	NA
pH	The pH of the solution is adjusted to 3.5 (range, 3.0 to 3.8).
Melting point/Freezing Point	NA
Initial Boiling Point/Boiling Point Range	NA
Flash Point	NA
Evaporation Rate	NA
Flammability (solid, gas)	NA
Upper/Lower Flammability or Explosive Limits	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Relative Density	NA
Solubility	NA
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined.
Chemical Stability	Stable under standard use and storage conditions.
Hazardous Reactions	Not determined
Conditions to Avoid	Not determined
Incompatibilities	Not determined
Hazardous Decomposition Products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and hydrogen chloride.
Hazardous Polymerization	Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity - Not determined for the product formulation. Information for the active ingredient is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Irinotecan Hydrochloride	100 100	LD50 LD50	Oral Oral	867 765-1045	mg/kg mg/kg	Rat Mouse
Irinotecan Hydrochloride	100 100 100	LD50 LD50 LD50	Intravenous Intravenous Intravenous	84 132 40	mg/kg mg/kg mg/kg	Rat Mouse Dog
Irinotecan Hydrochloride	100	LD50	Intraperitoneal	177	mg/kg	Mouse

LD50 is the dosage producing 50% mortality.

Occupational Exposure Potential	There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known.
Signs and Symptoms	None anticipated from normal handling of this product. During occupational use, this material should be considered irritating to the eyes and respiratory tract. In clinical use, adverse effects have included bone marrow suppression, nausea, vomiting, and acute diarrhea. Initially, diarrhea may occur within 24 hours as part of a cholinergic syndrome that can also include sweating, hyper-salivation, abdominal cramps, lachrymation, and miosis. After 24 hours, a more severe, prolonged life-threatening diarrhea can occur. Additional adverse effects may include asthenia, dizziness, anorexia; dermatological reactions such as rashes, alopecia; hepatic effects such as elevations in liver enzymes and bilirubin; pulmonary effects such as interstitial pneumonia and pneumonitis with coughing and dyspnea; and cardiovascular effects such as vasodilation, hypotension, and thromboemolic events. There are also infrequent reports of hypersensitivity reactions.
Aspiration Hazard	None anticipated from normal handling of this product.
Dermal Irritation/ Corrosion	None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with redness and discomfort.
Ocular Irritation/ Corrosion	None anticipated from normal handling of this product. However, inadvertent eye contact of this product with eyes may produce irritation with stinging, redness, watering, and discomfort.
Dermal or Respiratory Sensitization	None anticipated from normal handling of this product. In clinical use, hypersensitivity reactions have been reported infrequently.

11. TOXICOLOGICAL INFORMATION: continued

Reproductive Effects	None anticipated from normal handling of this product. In studies in animals, no significant adverse effects on fertility and general reproductive performance were observed after intravenous administration of irinotecan to rats and rabbits at dosages of up to 6 mg/kg/day. However, in repeat-dose studies, testicular atrophy was noted in rodents at a dosage of 20 mg/kg/day, and in dogs at a dosage of 0.4 mg/kg/day. Intravenous administration to rats and rabbits at a dosage of 6 mg/kg/day during organogenesis produced embryotoxicity characterized by increased post-implantation loss and decreased numbers of live fetuses. Irinotecan was teratogenic in rats at dosages greater than 1.2 mg/kg/day, and in rabbits at a dosage of 6.0 mg/kg/day. Irinotecan administered to rat dams for the period following organogenesis through weaning at dosage of 6 mg/kg/day caused decreased learning ability and decreased female body weights in the offspring.
Mutagenicity	Neither irinotecan nor its major metabolite was mutagenic in the *in vitro* Ames assay. Irinotecan was clastogenic both in vitro (chromosome aberrations in Chinese hamster ovary cells) and in vivo (micronucleus test in mice).
Carcinogenicity	Long-term carcinogenicity studies with irinotecan have not been conducted. However, intravenous administration of irinotecan to rats at dosages of 2 mg/kg or 25 mg/kg irinotecan once a week for 13 weeks, followed by recovery for 91 weeks, resulted in a significant dose-related trend for the incidence of combined uterine horn endometrial stromal polyps and endometrial stromal sarcomas.
Carcinogen Lists	**IARC:** Not listed **NTP:** Not listed **OSHA:** Not listed
Specific Target Organ Toxicity – Single Exposure	NA
Specific Target Organ Toxicity – Repeat Exposure	Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, cardiovascular system, lungs, and liver.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined for product.
Persistence/Biodegradability	Not determined for product.
Bioaccumulation	Not determined for product.
Mobility in Soil	Not determined for product.
General Notes	In product stability studies, a solution of irinotecan photodegraded rapidly (about 32% in 6 hours at pH 7.0). Irinotecan is not anticipated to persist in the aquatic environment.

13. DISPOSAL CONSIDERATIONS

Waste Disposal	All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements.
Container Handling and Disposal	Dispose of containers and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA

ICAO/IATA STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA

IMDG STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA

Notes: DOT - US Department of Transportation Regulations

15. REGULATORY INFORMATION

US TSCA Status	Exempt
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US PROP 65 (Calif.)	Not listed

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

GHS/CLP Classification*

*In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.

15. REGULATORY INFORMATION: continued

EU Classification*	*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.
Classification(s)	NA
Symbol	NA
Indication of Danger	NA
Risk Phrases	NA
Safety Phrases	S23: Do not breathe vapor/spray S24: Avoid contact with the skin S25: Avoid contact with eyes S37/39 Wear suitable gloves and eye/face protection.

16. OTHER INFORMATION

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD_{50}	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS
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